

Whole scope is clear of art.

10/553,937B Yong Chu 08-13-2007

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NEWS 6 MAY 21 TOXCENTER enhanced with BIOSIS reload
NEWS 7 MAY 21 CA/CAplus enhanced with additional kind codes for German patents
NEWS 8 MAY 22 CA/CAplus enhanced with IPC reclassification in Japanese patents
NEWS 9 JUN 27 CA/CAplus enhanced with pre-1967 CAS Registry Numbers
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NEWS 12 JUL 02 LEMBASE coverage updated
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NEWS 17 JUL 16 CAplus enhanced with French and German abstracts
NEWS 18 JUL 18 CA/CAplus patent coverage enhanced
NEWS 19 JUL 26 USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 20 JUL 30 USGENE now available on STN
NEWS 21 AUG 06 CAS REGISTRY enhanced with new experimental property tags
NEWS 22 AUG 06 BEILSTEIN updated with new compounds
NEWS 23 AUG 06 FSTA enhanced with new thesaurus edition
NEWS 24 AUG 13 CA/CAplus enhanced with additional kind codes for granted patents

NEWS EXPRESS 29 JUNE 2007: CURRENT WINDOWS VERSION IS V8.2,
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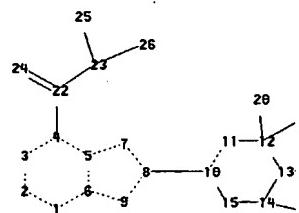
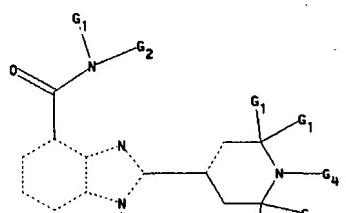
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chain nodes :
16 17 20 21 22 23 24 25 26 31 33
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
chain bonds :
4-22 8-10 9-31 12-20 12-21 13-33 14-16 14-17 22-23 22-24 23-25 23-26
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 10-11 10-15 11-12 12-13 13-14
14-15
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 9-31 10-11 10-15 11-12 12-13
12-20 12-21 13-14 13-33 14-15 14-16 14-17 22-23 22-24 23-25 23-26
exact bonds :
4-22 8-10

G1:CH3,CH2,CH,Et,n-Pr,i-Pr,n-Bu,i-Bu,s-Bu,H

G2:H,CH3,CH,Et,i-Bu,t-Bu,OH,MeO,EtO,n-PrO,i-PrO,n-BuO,i-BuO,s-BuO,t-BuO

G3:H,CH3,CH2,CH,Et,n-Pr,i-Pr,n-Bu,i-Bu,s-Bu,t-Bu,Cb

G4:H,O,N

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS 17:CLASS 20:CLASS 21:CLASS
22:CLASS 23:CLASS
24:CLASS 25:CLASS 26:CLASS 31:CLASS 33:CLASS

L1 STRUCTURE UPLOADED

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L1 HAS NO ANSWERS
L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s 11
SAMPLE SEARCH INITIATED 14:19:57 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 30 TO ITERATE

100.0% PROCESSED 30 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 272 TO 928
PROJECTED ANSWERS: 1 TO 80

L2 1 SEA SSS SAM L1

=> s 11 full
FULL SEARCH INITIATED 14:20:02 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 579 TO ITERATE

100.0% PROCESSED 579 ITERATIONS 11 ANSWERS
SEARCH TIME: 00.00.01

L3 11 SEA SSS FUL L1

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COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 172.55 172.76

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FILE LAST UPDATED: 12 Aug 2007 (20070812/ED)

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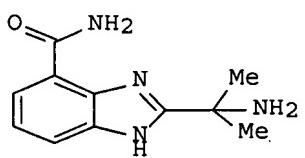
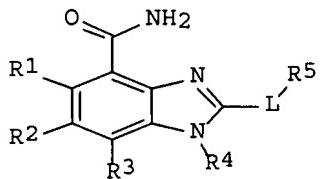
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L4 10 L3

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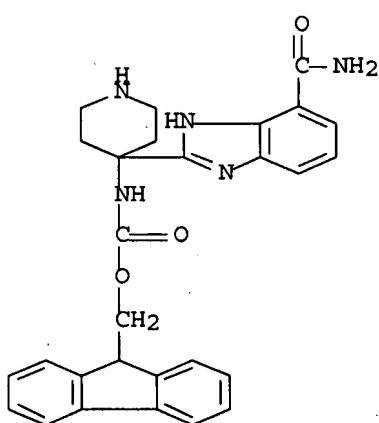
L4 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1070298 CAPLUS Full-text
DOCUMENT NUMBER: 145:419147
TITLE: Preparation of 2-substituted-1H-benzimidazole-4-carboxamides as PARP inhibitors for the treatment of inflammation, sepsis and septic shock
INVENTOR(S): Zhu, Gui-Dong; Gandhi, Virajkumar B.; Gong, Jianchun; Penning, Thomas D.; Giranda, Vincent L.; Thomas, Sheela
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 21pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| US 2006229351 | A1 | 20061012 | US 2006-401635 | 20060411 |
| WO 2006110683 | A1 | 20061019 | WO 2006-US13366 | 20060411 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM | | | | |

PRIORITY APPLN. INFO.: US 2005-670205P P 20050411
 OTHER SOURCE(S): MARPAT 145:419147
 GI



- AB Title compds. I [wherein R1 - R4 = H, alkyl, hydroxyalkyl, etc.; R5 = heteroaryl, heteroarylalkoxy, heteroaryloxy, etc.; L = alkylene, alkenylene, cycloalkylene, etc.] and therapeutically acceptable salts were prep'd. as poly(ADP-ribose)polymerase (PARP) inhibitors. For instance, amidation of 2-[(benzyloxy)carbonyl]amino]-2-methylpropanoic acid with 2,3-diaminobenzamide dihydrochloride followed by mol. cyclization in refluxing acetic acid and subsequent hydrogenolysis gave benzimidazolecarboxamide II. I were found to be active PARP inhibitors that can penetrate cell membranes. Therefore, the invented compds. and their pharmaceutical compns. are useful for treating diseases assocd. with PARP, including inflammation, sepsis and septic shock.
- IT 912336-22-2P
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (inhibitor; prepn. of benzimidazolecarboxamides as PARP inhibitors for treatment of inflammation, sepsis and septic shock)
- RN 912336-22-2 CAPLUS
- CN Carbamic acid, [4-[7-(aminocarbonyl)-1H-benzimidazol-2-yl]-4-piperidinyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)



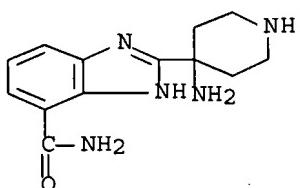
IT 912336-26-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(inhibitor; prepn. of benzimidazolecarboxamides as PARP inhibitors for treatment of inflammation, sepsis and septic shock)

RN 912336-26-6 CAPLUS

CN 1H-Benzimidazole-4-carboxamide, 2-(4-amino-4-piperidinyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1069940 CAPLUS Full-text

DOCUMENT NUMBER: 145:419145

TITLE: Preparation of 1H-benzimidazole-4-carboxamides as poly(ADP-ribose)polymerase (PARP) inhibitors.

INVENTOR(S): Zhu, Gui-Dong; Gong, Jianchun; Gandhi, Virajkumar B.; Penning, Thomas D.; Giranda, Vincent L.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 34pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

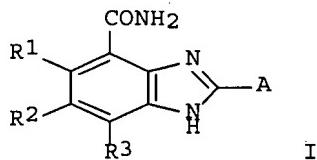
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2006229289 | A1 | 20061012 | US 2006-401638 | 20060411 |
| WO 2006110816 | A2 | 20061019 | WO 2006-US13652 | 20060411 |
| WO 2006110816 | A3 | 20070104 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
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 KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
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 VN, YU, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
 CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
 GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-670204P P 20050411

OTHER SOURCE(S): MARPAT 145:419145

GI



AB Title compds. [I; R1-R3 = H, alkyl, alkenyl, alkynyl, alkoxy, alkoxycarbonyl, cyano, haloalkoxy, haloalkyl, halo, OH, hydroxyalkyl, NO₂, amino, aminocarbonyl; A = nonarom. (substituted) 4-8 membered ring contg. 1-2 N atoms and optionally 1 S or O atom; A bears a Me group at the atom bonded to the imidazole ring], were prep'd. Thus, 2-(2-methylpyrrolidin-2-yl)-1H-benzimidazole-4-carboxamide (prepn. starting from 1-benzyl 2-Me pyrrolidine-1,2-dicarboxylate and 2,3-diaminobenzamide dihydrochloride given) inhibited PARP with IC₅₀ = 4.3 nM.

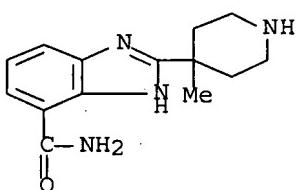
IT 912444-86-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of benzimidazolecarboxamides as PARP inhibitors)

RN 912444-86-1 CAPLUS

CN 1H-Benzimidazole-4-carboxamide, 2-(4-methyl-4-piperidinyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:44136 CAPLUS Full-text

DOCUMENT NUMBER: 144:225970

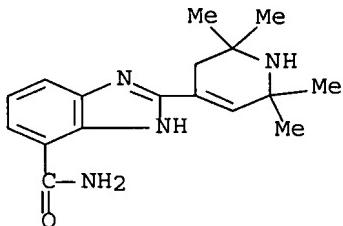
TITLE: Critical role of PI3-kinase/Akt activation in the PARP

AUTHOR(S): Kovacs, Krisztina; Toth, Ambrus; Deres, Peter; Kalai, Tamas; Hideg, Kalman; Gallyas, Ferenc; Sumegi, Balazs
 CORPORATE SOURCE: Research Group for Mitochondrial Function and Mitochondrial Diseases, Department of Biochemistry and Medical Chemistry/Hungarian Academy of Sciences, Hung.
 SOURCE: Biochemical Pharmacology (2006), 71(4), 441-452
 CODEN: BCPCA6; ISSN: 0006-2952
 PUBLISHER: Elsevier B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Poly(ADP-ribose) polymerase (PARP) inhibitors protect hearts from ischemia-reperfusion (IR)-induced damages by limiting NAD (NAD+) and ATP depletion, and by other, not yet elucidated mechanisms. Our preliminary data suggested that PARP catalyzed ADP-ribosylations may affect signaling pathways in cardiomyocytes. To clarify this possibility, we studied the effect of a well-characterized (4-hydroxyquinazoline) and a novel (carboxaminobenzimidazol-deriv.) PARP inhibitor on the activation of phosphatidylinositol-3-kinase (PI3-kinase)/Akt pathway in Langendorff-perfused hearts. PARP inhibitors promoted the restoration of myocardial energy metab. (assessed by ^{31}P NMR spectroscopy) and cardiac function compared to untreated hearts. PARP inhibitors also attenuated the infarct size and reduced the IR-induced lipid peroxidn., protein oxidn. and total peroxide concn. Moreover, PARP inhibitors facilitated Akt phosphorylation and activation, as well as the phosphorylation of its downstream target glycogen synthase kinase-3. β . (GSK-3. β .) in normoxia and, more robustly, during IR. Blocking PI3-kinase by wortmannin or LY294002 reduced the PARP inhibitor-elicited robust Akt and GSK-3. β . phosphorylation upon ischemia-reperfusion, and significantly diminished the recovery of ATP and creatine phosphate showing the importance of Akt activation in the recovery of energy metab. In addn., inhibition of PI3-kinase/Akt pathway decreased the protective effect of PARP inhibitors on infarct size and the recovery of heart functions. All these data suggest that contrary to the original view, which considered preservation of NAD+ and consequently ATP pools as the exclusive underlying mechanism for the cytoprotective effect of PARP inhibitors, the activation of PI3-kinase/Akt pathway and related processes are at least equally important in the cardioprotective effects of PARP inhibitors during ischemia-reperfusion.

IT 693803-52-0, HO-3089
 RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (crit. role of PI3-kinase/Akt signaling in PARP inhibitor induced heart function recovery during ischemia-reperfusion)

RN 693803-52-0 CAPLUS
CN 1H-Benzimidazole-4-carboxamide, 2-(1,2,3,6-tetrahydro-2,2,6,6-tetramethyl-4-pyridinyl)- (9CI) (CA INDEX NAME)



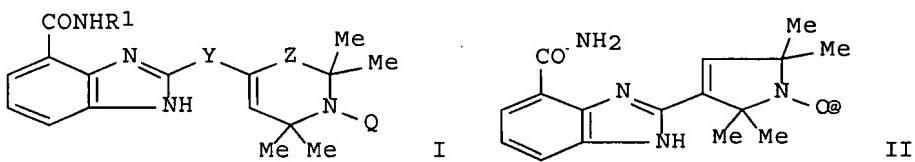
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:965241 CAPLUS Full-text Current
DOCUMENT NUMBER: 141:410928
TITLE: Preparation of alicyclic-amine-substituted
4-carboxamido-benzimidazoles for use in pharmaceutical
compositions as poly(ADP-ribose) polymerase (PARP)
inhibitors and antioxidants
INVENTOR(S): Hideg, Kalman; Kalai, Tamas; Suemegi, Balazs
PATENT ASSIGNEE(S): Hung.
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

Current app.

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------------|---|----------|-----------------|-----------------------------|
| WO 2004096793 | A1 | 20041111 | WO 2004-HU43 | <u>20040427</u> |
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CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
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SN, TD, TG | | | |
| EP 1622893 | A1 | 20060208 | EP 2004-729685 | 20040427 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | |
| US 2007072912 | A1 | 20070329 | US 2006-553937 | 20060921 |
| ORITY APPLN. INFO.: | | | HU 2003-1154 | A <u>20030428</u> + English |
| | | | WO 2004-HU43 | W <u>20040427</u> |

OTHER SOURCE(S) : MARPAT 141:410928
GI



AB Benzimidazoles, such as I [R1 = H, alkyl, alkoxy; Q = H, oxy; Y = bond or linking group, such as SCH₂, OCH₂, alkylene, etc.; Z = bond or CH₂;], were prep'd. for therapeutic use as PARP inhibitors and antioxidants. Thus, 2-[1-oxy-2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl]-1H-benzimidazole-4-

carboxamide (II) was prep'd. via a cyclocondensation reaction in 51% yield of 2,3-diaminobenzamide with 3-formyl-2,2,5,5-tetramethyl-1-oxypyrroline. The prep'd. benzimidazoles were assayed in vitro for PARP inhibitory activity and were assayed for inhibition of HO induced cell death in WRL-68 human liver cells.

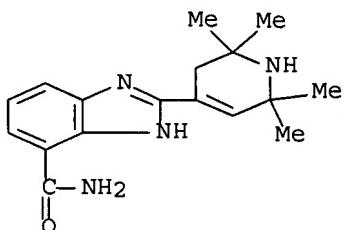
IT 693803-52-0P 791591-34-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of alicyclic-amine-substituted 4-carboxamido-benzimidazoles for use in pharmaceutical compns. as poly(ADP-ribose) polymerase (PARP) inhibitors and antioxidants)

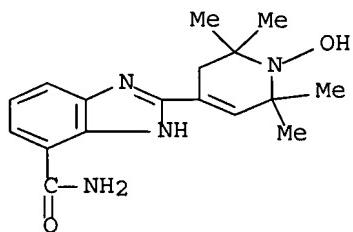
RN 693803-52-0 CAPPLUS

CN 1H-Benzimidazole-4-carboxamide, 2-(1,2,3,6-tetrahydro-2,2,6,6-tetramethyl-4-pyridinyl)- (9CI) (CA INDEX NAME)



RN 791591-34-9 CAPPLUS

CN 1H-Benzimidazole-4-carboxamide, 2-(1,2,3,6-tetrahydro-1-hydroxy-2,2,6,6-tetramethyl-4-pyridinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 10 CAPPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:538725 CAPPLUS Full-text

DOCUMENT NUMBER: 142:32704

TITLE: Myocardial protection by selective poly(ADP-ribose) polymerase inhibitors

AUTHOR(S): Kovacs, Krisztina; Toth, Ambrus; Deres, Peter; Kalai, Tamas; Hideg, Kalman; Sumegi, Balazs

CORPORATE SOURCE: Department of Biochemistry and Medical Chemistry, Faculty of Medicine, University of Pecs, Pecs, Hung.

SOURCE: Experimental & Clinical Cardiology (2004), 9(1), 17-20

CODEN: ECCAF7; ISSN: 1205-6626

PUBLISHER: Pulsus Group Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB During ischemia-reperfusion, reactive oxygen species are generated along the mitochondrial respiratory chain and induce lipid peroxidn., protein oxidn. and DNA damage. Single-strand DNA breaks are the most potent activators of poly(ADP-ribose) polymerase (PARP); prolonged action of PARP culminates in intracellular oxidized NAD (NAD+) and ATP depletion. The integrity of cellular components and the myocardial energy metab. can be preserved by using PARP inhibitors under conditions of ischemia and reperfusion. Oxidative stress is capable of activating the phosphoinositol-3-kinase-Akt/protein kinase B signaling pathway, which is further enhanced if treated with PARP inhibitors. Akt, in turn, promotes the survival of cardiomyocytes by inhibiting apoptosis, and causing metabolic adjustment and vasodilation in the jeopardized myocardium.

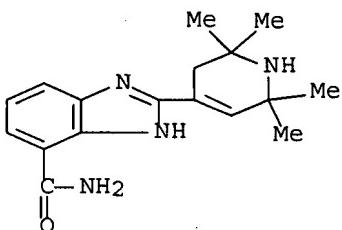
IT 693803-52-0, HO 3089

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(poly(ADP-ribose) polymerase inhibitor HO-3089 improved recovery of inorg. phosphates, myocardial energy metab., Akt activation, attenuated oxidative injury during ischemia-reperfusion in rat heart)

RN 693803-52-0 CAPLUS

CN 1H-Benzimidazole-4-carboxamide, 2-(1,2,3,6-tetrahydro-2,2,6,6-tetramethyl-4-pyridinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

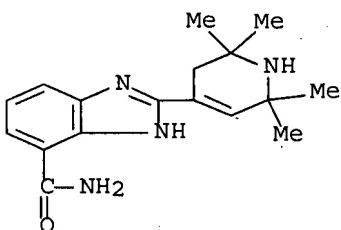
L4 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:511475 CAPLUS Full-text
DOCUMENT NUMBER: 142:16741
TITLE: Hemorheological methods in drug research
AUTHOR(S): Marton, Zsolt; Halmosi, Robert; Alexy, Tamas; Horvath, Beata; Toth, Ambrus; Feher, Gergely; Koltai, Katalin; Kesmarky, Gabor; Habon, Tamas; Sumegi, Balazs; Hideg, Kalman; Toth, Kalman
CORPORATE SOURCE: 1st Department of Medicine Division of Cardiology, University of Pecs Medical School, Hung.
SOURCE: Clinical Hemorheology and Microcirculation (2004), 30(3,4), 243-252
PUBLISHER: IOS Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Development of new drugs is a sophisticated process that requires several, different methods. In our expts. we have applied two rheol. models to study exptl. and clin. used drugs. The antioxidant properties of several agents were estd. by erythrocyte filtration technique. The known antioxidant compd. vitamin E was used to validate our measurements. An exptl. cardioprotective agent, H-2545 provided significant protection against oxidative changes in red blood cell filterability ($p<0.001$). Although some of the examd., known cardiovascular drugs also showed significant antioxidant effect, they were less efficient than H-2545 and the scavenger effect of this novel agent exceeded the antioxidant properties of vitamin E. Modification of mexiletine with a pyrrolidine ring improved significantly its antioxidant capacity suggesting this mol. segment to be responsible for the antioxidant effect. In our second model the antiplatelet effect of exptl. poly(ADP-ribose) polymerase (PARP) inhibitors was evaluated. Two widely used antiplatelet agents, i.e. acetyl salicylic acid and eptifibatide, served as controls in the validation of the measurements. PARP inhibitors reduced ADP-induced platelet aggregation in a dose-dependent manner ($p<0.05$). However, their hindrance on platelet aggregation waned as the concn. of ADP rose. Regarding the platelets role in the development of ischemic vascular diseases, the antiaggregating property of PARP inhibitors may exert addnl. beneficial effects on tissue blood supply under conditions of compromised vascular flow.

IT 693803-52-0, HO 3089
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HO-3089 showed marked inhibition of platelet aggregation in PMS-treated human RBC)

RN 693803-52-0 CAPLUS

CN 1H-Benzimidazole-4-carboxamide, 2-(1,2,3,6-tetrahydro-2,2,6,6-tetramethyl-4-pyridinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:270493 CAPLUS Full-text
DOCUMENT NUMBER: 141:836
TITLE: Inhibition of ADP-evoked platelet aggregation by selected poly(ADP-ribose) polymerase inhibitors
AUTHOR(S): Alexy, Tamas; Toth, Ambrus; Marton, Zsolt; Horvath, Beata; Koltai, Katalin; Feher, Gergely; Kesmarky, Gabor; Kalai, Tamas; Hideg, Kalman; Sumegi, Balazs; Toth, Kalman
CORPORATE SOURCE: First Department of Medicine, Division of Cardiology, Medical School, University of Pecs, Pecs, 7624, Hung.
SOURCE: Journal of Cardiovascular Pharmacology (2004), 43(3), 423-431

102A

3/2004

CODEN: JCPCDT; ISSN: 0160-2446

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Pathol. platelet activation has been implicated in the pathogenesis of ischemic heart disease. Since cardiomyocytes can be protected from ischemia-reoxygenation injury by poly(ADP-ribose) polymerase (PARP) inhibitors mimicking the adenine/ADP part of NAD⁺, their structural resemblance to ADP may also enable the blockade of platelet aggregation via binding to ADP receptors. Blood samples drawn from healthy volunteers were pre-incubated with different concns. of PARP inhibitors: 4-hydroxyquinazoline, 2-mercaptop-4(3H)-quinazolinone, or HO-3089. ADP-, collagen- and epinephrine-induced platelet aggregation was evaluated according to the method described by Born. The effect of PARP inhibitors on thrombocyte aggregation was also examd. when platelets were sensitized by heparin and in the presence of incremental concns. of ADP. All examd. PARP inhibitors reduced the ADP-induced platelet aggregation in a dose-dependent manner (significant inhibition at 20 .mu.M for HO-3089 and at 500 .mu.M for the other agents; P < 0.05), even if platelets were sensitized with heparin. However, their hindrance on platelet aggregation waned as the concn. of ADP rose (no effect at 40 .mu.M ADP). PARP inhibitors had minimal effect on both collagen- and epinephrine-induced platelet aggregation. Our study first demonstrates the feasibility of a design for PARP inhibitors that does not only protect against ischemia-reperfusion-induced cardiac damage but may also prevent thrombotic events.

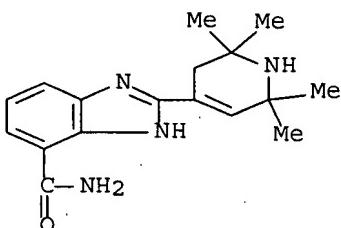
IT 693803-52-0, HO 3089

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibition of ADP-evoked platelet aggregation by selected poly(ADP-ribose) polymerase inhibitors)

RN 693803-52-0 CAPLUS

CN 1H-Benzimidazole-4-carboxamide, 2-(1,2,3,6-tetrahydro-2,2,6,6-tetramethyl-4-pyridinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:676008 CAPLUS Full-text

DOCUMENT NUMBER: 137:216949

TITLE: Preparation of benzimidazole derivatives as poly(ADP-ribose) polymerase (PARP) inhibitors

INVENTOR(S): Takayama, Kazuhisa; Kimura, Takenori; Masuda, Naoyuki; Naito, Ryo; Okamoto, Yoshinori; Koga, Yuji; Okada, Yohei; Takeuchi, Makoto

PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

Japanese

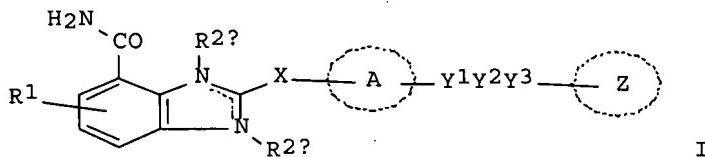
FAMILY ACC. NUM. COUNT:

1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2002068407 | A1 | 20020906 | WO 2002-JP1741 | 20020226 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2002233746 | A1 | 20020912 | AU 2002-233746 | 20020226 |
| PRIORITY APPLN. INFO.: | | | JP 2001-54693 | A 20010228 |
| | | | WO 2002-JP1741 | W 20020226 |

OTHER SOURCE(S): MARPAT 137:216949
GI



AB The title compds. I [R1 = H, alkyl, etc.; R2a, R2b = H, alkyl, or nonexistent; the dotted line indicates the double bond or single bond; ring A = N-contg. satd. heterocyclic ring; X = (oxo-substituted) alkylene, or bond; Y1, Y3 = (oxo-substituted) alkylene, etc.; Y2 = O, S, etc.; ring Z = (un)substituted cycloalkyl, etc.; provisos are given] are prep'd. 2-[1-[4-(4-Fluorophenoxy)butyl]piperidin-4-yl]-1H-benzimidazole-4- carboxamide 2HCl salt in vitro showed IC50 of 8.2 nM against poly(ADP-ribose) polymerase.

IT 454715-39-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of benzimidazole derivs. as poly(ADP-ribose) polymerase inhibitors)

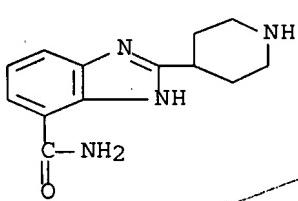
RN 454715-39-0 CAPLUS

CN 1H-Benzimidazole-4-carboxamide, 2-(4-piperidinyl)-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

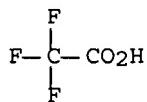
CRN 272769-47-8

CMF C13 H16 N4 O



CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

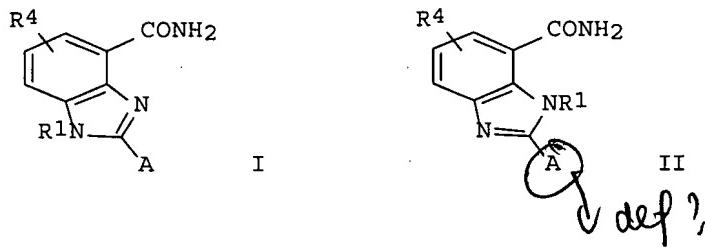
L4 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2000:384161 CAPLUS Full-text
 DOCUMENT NUMBER: 133:17464
 TITLE: Preparation of benzimidazolecarboxamides as poly(ADP-ribose)polymerase inhibitors.
 INVENTOR(S): Lubisch, Wilfried; Kock, Michael; Hoger, Thomas;
 Schult, Sabine; Grandel, Roland; Muller, Reinhold
 PATENT ASSIGNEE(S): Basf Aktiengesellschaft, Germany
 SOURCE: PCT Int. Appl., 44 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

10/935,683
6/8/2006

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|----------|
| WO 2000032579 | A1 | 20000608 | WO 1999-EP9004 | 19991123 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 19916460 | A1 | 20001019 | DE 1999-19916460 | 19990412 |
| DE 19916460 | B4 | 20061221 | | |
| CA 2352554 | A1 | 20000608 | CA 1999-2352554 | 19991123 |
| CA 2352554 | C | 20061010 | | |
| BR 9915701 | A | 20010814 | BR 1999-15701 | 19991123 |

| | | | | |
|--|----|----------|-----------------------|-----------------|
| EP 1133477 | A1 | 20010919 | EP 1999-964497 | 19991123 |
| EP 1133477 | B1 | 20040218 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO | | | | |
| TR 200101498 | T2 | 20011121 | TR 2001-200101498 | 19991123 |
| HU 200200749 | A2 | 20020828 | HU 2002-749 | 19991123 |
| HU 200200749 | A3 | 20030328 | | |
| JP 2002531442 | T | 20020924 | JP 2000-585221 | 19991123 |
| JP 3432800 | B2 | 20030804 | | |
| AU 764216 | B2 | 20030814 | AU 2000-30343 | 19991123 |
| NZ 511825 | A | 20030829 | NZ 1999-511825 | 19991123 |
| AT 259789 | T | 20040315 | AT 1999-964497 | 19991123 |
| PT 1133477 | T | 20040630 | PT 1999-964497 | 19991123 |
| ES 2216625 | T3 | 20041016 | ES 1999-964497 | 19991123 |
| SK 285529 | B6 | 20070301 | SK 2001-714 | 19991123 |
| TW 247741 | B | 20060121 | TW 1999-88120715 | 19991126 |
| ZA 2001004118 | A | 20020521 | ZA 2001-4118 | 20010521 |
| MX 2001PA05197 | A | 20020108 | MX 2001-PA5197 | 20010524 |
| <u>US 6448271</u> | B1 | 20020910 | <u>US 2001-856686</u> | 20010524 |
| <u>US 39608</u> | E1 | 20070501 | <u>US 2001-935683</u> | <u>20010524</u> |
| NO 2001002570 | A | 20010713 | NO 2001-2570 | 20010525 |
| IN 2001CN00730 | A | 20050304 | IN 2001-CN730 | 20010525 |
| BG 105596 | A | 20020228 | BG 2001-105596 | 20010613 |
| BG 65047 | B1 | 20070131 | | |
| HR 2001000484 | A1 | 20030430 | HR 2001-484 | 20010626 |
| HK 1042084 | A1 | 20050902 | HK 2002-103400 | 20020504 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | DE 1998-19854933 | A 19981127 |
| | | | DE 1999-19916460 | A 19990412 |
| | | | WO 1999-EP9004 | W 19991123 |
| | | | US 2001-856686 | E 20010524 |

OTHER SOURCE(S): MARPAT 133:17464
GI



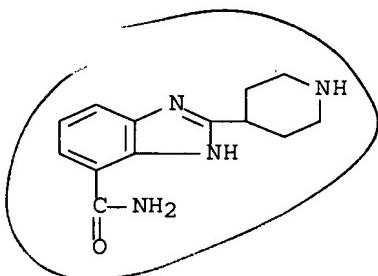
AB Title compds. [I, II; R1 = H, (substituted) (O- or imino-interrupted) alkyl; R4 = H, alkyl, Cl, Br, F, NO₂, cyano, amino, acylamino, etc.; A = (unsatd.) 4-8 membered (substituted) heterocycl], were prep'd. as PARP inhibitors (no data). Thus, 1-(tert-butoxycarbonyl)piperidine-4-carboxylic acid, Et 2,3-diaminobenzoate, Et₃N, and hydroxybenzotriazole in THF at 0.degree. were treated with N'-(3-dimethylaminopropyl)-N- ethylcarbodiimide followed by 24 h stirring to give N-(2-amino-3- ethoxycarbonyl)-1-(tert-butoxycarbonyl)piperidine-4-carboxanilide. This was refluxed 30 min. in HOAc to give Et 2-[1-(tert- butoxycarbonyl)piperidin-4-yl]benzimidazole-4-carboxylate, which was converted to 2-piperidin-4-ylbenzimidazole-4-carboxamide dihydrochloride.

IT 272769-46-7P 272769-47-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of benzimidazolecarboxamides as poly(ADP-ribose)polymerase
inhibitors)

RN 272769-46-7 CAPLUS

CN 1H-Benzimidazole-4-carboxamide, 2-(4-piperidinyl)-, dihydrochloride (9CI)
(CA INDEX NAME)



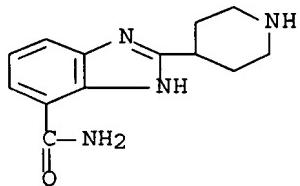
103A

rejection?

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RN 272769-47-8 CAPLUS

CN 1H-Benzimidazole-4-carboxamide, 2-(4-piperidinyl)- (9CI) (CA INDEX NAME)

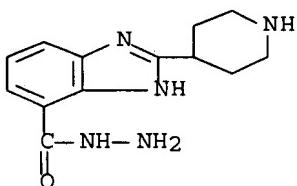


IT 272769-72-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. of benzimidazolecarboxamides as poly(ADP-ribose)polymerase
inhibitors)

RN 272769-72-9 CAPLUS

CN 1H-Benzimidazole-4-carboxylic acid, 2-(4-piperidinyl)-, hydrazide (9CI)
(CA INDEX NAME)



REFERENCE COUNT:

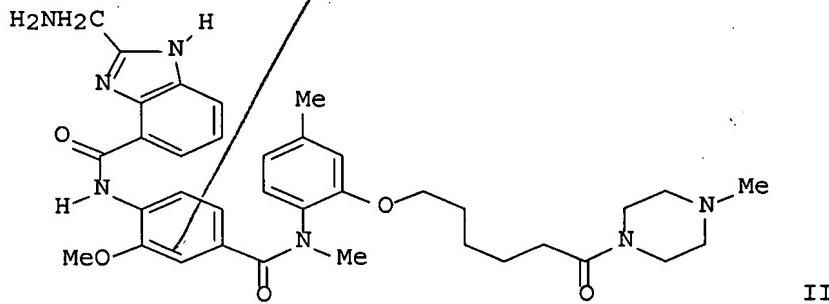
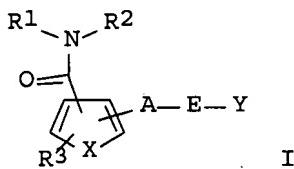
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THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1998:394328 CAPLUS Full-text
 DOCUMENT NUMBER: 129:67773
 TITLE: Preparation of benzamide derivatives having a
 vasopressin antagonistic activity
 INVENTOR(S): Setoi, Hiroyuki; Ohkawa, Takehiko; Zenkoh, Tatsuya;
 Sawada, Hitoshi; Sawada, Yuki; Oku, Teruo
 PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 332 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|-------------|
| WO 9824771 | A1 | 19980611 | WO 1997-JP4192 | 19971118 |
| W: AU, CA, CN, HU, IL, JP, KR, MX, US, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9749672 | A | 19980629 | AU 1997-49672 | 19971118 |
| EP 946519 | A1 | 19991006 | EP 1997-912493 | 19971118 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| JP 2001505193 | T | 20010417 | JP 1998-521225 | 19971118 |
| US 6207693 | B1 | 20010327 | US 1999-308662 | 19990602 |
| US 6316482 | B1 | 20011113 | US 2000-614132 | 20000711 |
| PRIORITY APPLN. INFO.: | | | AU 1996-3953 | A 19961202 |
| | | | WO 1997-JP4192 | W 19971118 |
| | | | US 1999-308662 | A3 19990602 |

OTHER SOURCE(S): MARPAT 129:67773
 GI



AB The title compds. [I; R1 = (un)substituted aryl, cyclo(lower)alkyl, heterocyclyl; R2 = H, lower alkyl, etc.; R3 = H, halo, OH, etc.; A = a single bond, O, NH; E = lower alkylene, lower alkenylene, etc.; X = CH₂CH, CH:N, S; Y = (un)substituted aryl, condensed heterocyclyl, etc.] and their pharmaceutically acceptable salts, useful in treatment and/or prevention of hypertension, heart failure, renal insufficiency, edema, ascites, vasopressin parasecretion syndrome, hepatocirrhosis, hyponatremia, hypokalemia, diabetic, circulation disorder, cerebrovascular disease, Meniere's disease or motion sickness, were prep'd. Thus, the title compd. II showed IC50 of 1.5 nM against vasopressin 1 receptor binding.

IT 208770-38-1P 208771-48-6P

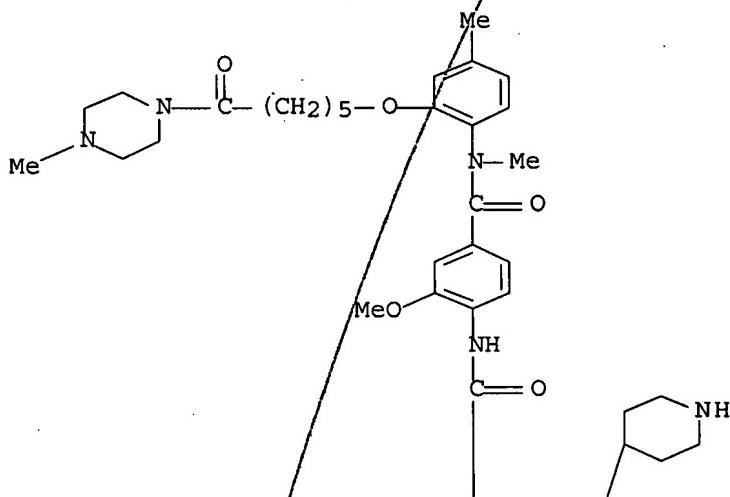
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of benzamide derivs. having a vasopressin antagonistic activity)

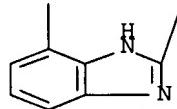
RN 208770-38-1 CAPPLUS

CN 1H-Benzimidazole-4-carboxamide, N-[2-methoxy-4-[[methyl[4-methyl-2-[[6-(4-methyl-1-piperazinyl)-6-oxohexyl]oxy]phenyl]amino]carbonyl]phenyl]-2-(4-piperidinyl)- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

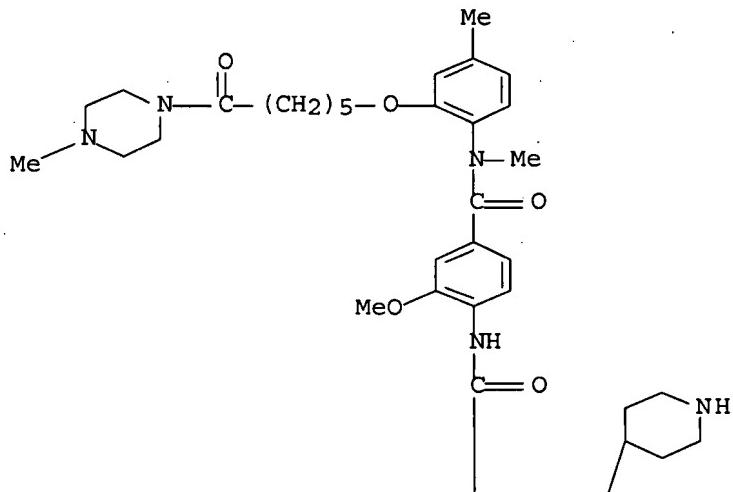


RN 208771-48-6 CAPPLUS

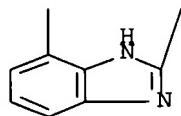
CN 1H-Benzimidazole-4-carboxamide, N-[2-methoxy-4-[[methyl[4-methyl-2-[[6-(4-methyl-1-piperazinyl)-6-oxohexyl]oxy]phenyl]amino]carbonyl]phenyl]-2-(4-

piperidinyl)-, trihydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



●3 HCl

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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Executing the logoff script...

=> LOG H

COST IN U.S. DOLLARS
FULL ESTIMATED COST

SINCE FILE
ENTRY
53.17

TOTAL
SESSION
225.93

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
CA SUBSCRIBER PRICE

SINCE FILE
ENTRY
-7.80

TOTAL
SESSION
-7.80

SESSION WILL BE HELD FOR 120 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 14:20:45 ON 13 AUG 2007